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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/943,780	08/30/2001	Kevin P. Baker	P2548P1C10	2570

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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	PAPER NUMBER
1643	
MAIL DATE	DELIVERY MODE
08/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/943,780	BAKER ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-26 and 35-36 are cancelled.

2. Claims 27-34 are pending and under consideration.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections Maintained

Claim Rejections - 35 USC §§ 101, 112

4. The rejection of claims 27-34 under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility is maintained.

Applicants maintain that the specification (pg. 119) provides evidence that the PRO357 gene is amplified in tumors and that one of ordinary skill in the art would find it credible that PRO357 has a diagnostic utility. Applicant states that the PTO has recognized that Applicants' asserted utility is sufficient by issuing U.S. Patent 7,208,308 (the "308 patent") with claims supported by the same utility as the utility asserted herein. Applicants' arguments have been fully considered but are not found persuasive. Applicant is reminded that each application is examined on its own merits. Further, every patent is presumed to be valid under the first sentence of 35 U.S.C. 282. Public policy demands that every employee of the United States Patent and Trademark Office (USPTO) refuse to express to any person any opinion as to the validity or invalidity of, or the patentability or unpatentability of any claim in any U.S. patent, except to the extent necessary to carry out

(A) an examination of a reissue application of the patent,

(B) a reexamination proceeding to reexamine the patent, or

(C) an interference involving the patent.

The question of validity or invalidity is otherwise exclusively a matter to be determined by a court. Likewise, the question of enforceability or unenforceability is

exclusively a matter to be determined by a court. Thus, the examiner is precluded from commenting on the '308 patent and applicants' arguments thereto.

Applicant argues that the declarations of Paul Polakis and Randy Scott provide evidence supporting applicants' asserted utility when viewed in the proper context. Applicant asserts that the nature of the fact sought to be established in the Polakis and Scott Declarations is that under the proper utility standard, which only requires a fact be more likely true than not, the gene amplification observed for PRO357 more likely than not correlates to overexpression of the PRO357 polypeptide. Applicant points to Exhibit B of the second Polakis Declaration identifies 28 gene transcripts out of 31 gene transcripts (i.e., greater than 90%) that showed good correlation between tumor mRNA and tumor protein levels. Applicants' arguments have been fully considered but are not found persuasive. The examiner maintains that the nature of the fact to be established is whether PRO357 polypeptide expression is elevated in tumors, given that the claims are drawn to the PRO357 polypeptide. Again, like the first and second Polakis declarations, the Scott Declaration does not provide any data concerning PRO357 mRNA expression, PRO357 polypeptide expression, or the correlation between the two in tumor tissue and normal tissue. The fact that there may be a commonly understood general rule or dogma that increased mRNA levels are predictive of corresponding increased levels of the encoded protein does not establish the correlation between the change, if any, in PRO357 transcripts and PRO357 polypeptide expression in tumors because there are examples of genes for which such a correlation does not exist, as evidenced by the first and second Polakis declarations and the Scott declaration, which states "Although there are some exceptions on an individual gene basis...". Without any evidence of PRO357 mRNA or PRO357 polypeptide expression the Scott and Polakis declarations are of no avail to Applicants. Applicants' stance that it is more likely than not for amplified genes to have increased mRNA and protein levels because, in general, gene amplification increases mRNA expression and in turn, increased polypeptide levels is not found persuasive. Unlike the situations wherein a claimed compound has been tested and has shown a pharmacological activity and therefore has a therapeutic utility sufficient under the patent laws, or wherein an invention has only

limited utility and is only operable in certain applications and therefore has some degree of utility sufficient for patentability, in the present situation Applicants have not provided any testing of PRO357 mRNA or PRO357 polypeptide expression. In the absence of any information on the role, activity or expression of the PRO357 polypeptide in cancer, the examiner therefore considers the asserted utilities to not be specific and substantial because the skilled artisan would not know if or how PRO357 polypeptide expression changes in cancer. Applicants' utility standard would mandate only a showing that it is "not implausible" that the invention will work for its intended purpose. If mere plausibility were the test for how to use a claimed invention, Applicants could obtain patent rights to "inventions" based on a disclosure consisting of little more than guesses as to the likelihood of their success. When one of the guesses later proved true, the "inventor" would be rewarded the spoils instead of the party who demonstrated that the method actually worked. A probable utility does not establish a practical utility, which is established by actual testing or where the utility can be "foretold with certainty." *Bindra v. Kelly*, 206 USPQ 570, 575 (Bd. Pat. Inter. 1979) (Reduction to practice was not established for an intermediate useful in the preparation of a second intermediate with a known utility in the preparation of a pharmaceutical. The record established there was a high degree of probability of a successful preparation because one skilled in the art may have been motivated, in the sense of 35 U.S.C. 103, to prepare the second intermediate from the first intermediate. However, a strong probability of utility is not sufficient to establish practical utility.). Practical utility is a shorthand way of attributing "real-world" value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner, which provides some immediate benefit to the public. Credibility has never been questioned.

The specification does not disclose enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention. Therefore, the disclosure that PRO357 gene is amplified in tumor tissue (lung and colon) as compared to normal tissue does not impute a specific and substantial utility to the PRO357 polypeptide. Based on the present disclosure, one skilled in the art would be required to carry out further research to identify or reasonably

confirm a "real world" context of use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. Thus, the present disclosure is simply a starting point for further research and investigation into potential practical uses of the claimed polynucleotides. See *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), wherein the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an Appellant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Applicants' arguments that Pennica shows that for 2 of 3 genes studied, a positive correlation between gene amplification and protein overexpression and Ornoft reports that **in general** (18 of 23) chromosomal areas with more than 2-fold gain of DNA showed a corresponding increase in mRNA transcripts and applicants' arguments regarding Hyman and Pollack are acknowledged. Applicant states that Godbout teaches that a DEAD box gene, DDX1, shows good correlation between gene copy number, DDX1 transcript levels, and DDX1 protein levels in all cancer cell lines studied. Applicant argues that Zhigang ('Ziang'), Alberts and Lewin support applicants' assertion that in general it is more likely than not that there is a correlation between gene amplification an protein overexpression and these references should not be rejected because according to the PTO standards of utility, which only requires that the asserted utility is more likely than not true, not necessarily true.

Applicants' arguments have been fully considered but they are not persuasive. In the present case, applicants have not tested PRO357 mRNA or PRO357 polypeptide expression. The fact that there may be a general correlation between mRNA and protein does not tell the skilled artisan if the reported PRO357 gene amplification is associated with a corresponding increase in PRO357 polypeptide expression. Instead, Applicants merely propose a utility that is "not implausible," relying on a general

correlation between gene amplification and polypeptide expression rather than provide evidence of PRO357 polypeptide expression. Without any evidence of PRO357 polypeptide expression this reliance on a general correlation is of no avail to applicants because applicants have not established if the disclosed amplification of the PRO357 gene is one of those cases where the PRO357 polypeptide is overexpressed.

Applicants' arguments pertaining to Pennica, Ornoft, Hyman and Pollack have been fully considered but they are not persuasive. Pennica, Orntoft, Hyman and Pollack are evidence that at the time of applicants invention one would not know if PRO357 gene amplification is positively correlated with PRO357 polypeptide expression. Applicants have not established that the disclosed amplification of the PRO357 gene is one of those cases wherein the PRO357 polypeptide is overexpressed. Applicants have not tested PRO357 mRNA expression. Applicants have not tested PRO357 polypeptide expression. Gene expression is, admittedly, quite complicated (Meric, page 971, right column, first paragraph of "Introduction"). Pennica, Orntoft, Hyman and Pollack suffice to show that that DNA amplifications are not always associated with overexpression of the gene product and provide evidence that one with skill in the art would not accept the alleged utility of the PRO357 polypeptide and the claimed antibodies that bind it as obviously valid and correct.

Regarding Godbout, the examiner is aware of no evidence that in the time elapsed since 1987 or 1992 ERBA becomes overexpressed despite amplification in breast tumors or GADD153, GLI, and A2MR become commonly overexpressed in gene-amplified malignant gliomas. Godbout suffices to show that that DNA amplifications are not always associated with overexpression of the gene product and provide evidence that one with skill in the art would not accept the alleged utility of the PRO357 polypeptide and the claimed antibodies that bind it as obviously valid and correct.

Again, a probable utility does not establish a practical utility, which is established by actual testing or where the utility can be "foretold with certainty." *Bindra v. Kelly*, 206 USPQ 570, 575 (Bd. Pat. Inter. 1979) (Reduction to practice was not established for an intermediate useful in the preparation of a second intermediate with a known utility in the preparation of a pharmaceutical. The record established there was a high degree of

probability of a successful preparation because one skilled in the art may have been motivated, in the sense of 35 U.S.C. 103, to prepare the second intermediate from the first intermediate. However, a strong probability of utility is not sufficient to establish practical utility.). Practical utility is a shorthand way of attributing "real-world" value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner, which provides some immediate benefit to the public.

Applicants are not being asked to prove the asserted diagnostic utility either as a matter of statistical certainty or beyond a reasonable doubt. Rather, the fact to be established is whether there is a change in PRO357 polypeptide expression in tumors. The specification does not establish if the disclosed PRO357 gene amplification is one of those cases where there is a correlation between gene amplification and polypeptide expression. Applicants have not provided any testing of PRO357 mRNA expression or PRO357 polypeptide expression. Therefore, there is no reason for a skilled artisan to be reasonably convinced that the PRO357 polypeptide will exhibit the asserted diagnostic behavior. In the absence of any testing of the expression of the PRO357 polypeptide, the specification does not provide some immediate benefit to the public for the PRO357 polypeptide. None of Applicants' exhibits, arguments or declarations establish if or how expression of PRO357 mRNA, the PRO357 polypeptide, or any of the other claimed polypeptides, changes in tumor tissue as compared to normal tissue. Instead, Applicants merely propose a utility that is "not implausible," relying on a general correlation gene amplification and mRNA expression extrapolated to another general correlation between mRNA expression and expression of the encoded protein without any evidence of the PRO357 mRNA or PRO357 polypeptide expression. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695 (An invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form.). Based on the present disclosure, one skilled in the art would be required to carry out further research to identify or reasonably confirm a "real world" context of use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. Thus, the present disclosure is simply a starting point for further

research and investigation into potential practical uses of the claimed PRO357 polypeptide. See Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), wherein the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an Appellant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."
>
> For these reasons and those already of record, the rejection is maintained.

5. The rejection of claims 27-34 under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention is maintained.

Applicant's arguments have been fully considered but they are not persuasive. As Applicants recognize, a rejection under § 112, first paragraph, may be maintained on the same basis as a lack of utility rejection under § 101. A deficiency under 35 U.S.C. 101 also creates a deficiency under 35 U.S.C. 112, first paragraph. If the application fails as a matter of fact to satisfy 35 U.S.C. § 101, then the application also fails as a matter of law to enable one of ordinary skill in the art to use the invention under 35 U.S.C. § 112. Obviously, if a claimed invention does not have utility, the specification cannot enable one to use it. As such, a rejection properly imposed under 35 U.S.C. 101 should be accompanied with a rejection under 35 U.S.C. 112, first paragraph. The 35 U.S.C. 112, first paragraph, rejection set out a separate rejection that incorporates by reference the factual basis and conclusions set forth in the 35 U.S.C. 101 rejection. A 35 U.S.C. 112, first paragraph, rejection should be imposed or maintained when an appropriate basis exists for imposing a rejection under 35 U.S.C. 101.

6. The rejection of claims 27-34 under 35 U.S.C. 102(b) as being anticipated by Bostein et al (WO 99/35170, published 7/15/1999) is maintained.

Applicants' argue that the present application is entitled to the filing date of priority application 60/113,296, i.e., 12/22/1998, which discloses the PRO357 polypeptide and amino acid sequence as well as the gene amplification experiment described in Example 28 of the present specification is described in Example 2 of the '296 application. According to applicant, for the reasons discussed above, description of the gene amplification in the '296 application satisfies the utility and enablement requirements for the PRO357 polypeptide. This has been fully considered but is not found persuasive for the following reasons.

Under 35 U.S.C. 120, the claims in a U.S. application are entitled to the benefit of the filing date of an earlier filed U.S. application if the subject matter of the claim is disclosed in the manner provided by 35 U.S.C. 112, first paragraph in the earlier filed application. Under 35 U.S.C. 119 (a) or (e), the claims in a U.S. application are entitled to the benefit of a foreign priority date or the filing date of a provisional application if the corresponding foreign application or provisional application supports the claims in the manner required by 35 U.S.C. 112, first paragraph. A deficiency under 35 U.S.C. 101 also creates a deficiency under 35 U.S.C. 112, first paragraph.

Therefore, the claims are not entitled to the benefit of the filing date of the earlier filed applications because the subject matter of the present claims is not disclosed in the manner provided by 35 U.S.C. 112, first paragraph, in the earlier filed applications for the reasons set forth above in the rejections. Accordingly, the effective filing date for the claimed invention is 8/30/2001, which is the filing date of the instant application and the rejection is maintained.

7. No claims are allowable.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643